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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/362,485	07/28/99	FLOHE	L 29473/35834

HM12/1005

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EXAMINER	
JOHANNSEN, D	
ART UNIT	**PAPER NUMBER**
1655	20
DATE MAILED:	10/05/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/362,485	Flohe et al
Examiner	**Art Unit**
Diana Johannsen	1655

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jul 27, 2001* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-8 and 10-18* is/are pending in the application.

4a) Of the above, claim(s) *2-8 and 10-18* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

1. The Request for Continued Examination (RCE) under 37 C.F.R. 1.114 filed July 27, 2001 in application no. 09/362,485 is acceptable.

2. The Amendment filed June 27, 2001, paper no. 16, has been entered. Claim 1 has been amended and is now under consideration. Claims 2-8 and 10-18 have been withdrawn.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Election/Restriction

4. Claims 2-8 and 10-18 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 10.

5. It is noted that the restriction requirement was deemed proper and made final in the Office action of paper no. 11.

Claim Rejections - 35 U.S.C. § 112

6. Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claim is drawn to a "diagnostic kit" comprising an "enzymatic test kit" and a nucleic acid. However, while the specification as originally filed teaches both the enzymatic test kit and the nucleic acid sequences set forth in the claim, the specification does not disclose a diagnostic kit comprising both of these components, as required by the claim. In fact, no kit comprising the nucleic acids of instant claim 1, alone or in combination with any other reagents, is disclosed. Further, the specification does not disclose any other product or entity that could be considered equivalent to the product of claim 1 (e.g., the specification does not refer to a container or similar structure including all the components now set forth in claim 1). It is also noted that the specification does disclose not a method in which the claimed combination of components is employed. Accordingly, the specification does not provide basis for the diagnostic kit of claim 1.

7. Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite over the recitation of the language "hybridizable therewith". Neither the specification nor the teachings of the art provide a clear and limiting definition of this terminology, and it is unclear as to what types of relationships between nucleic acids would be encompassed by this language. Particularly, it is unclear as to whether Applicants intend for this language to encompass only sequences that actually hybridize to each other under the recited conditions (as would be indicated by language such as "sequences that hybridize thereto..."), or whether the use of the language "hybridizable therewith" is intended to indicate that there is, e.g.,

potential for hybridization or that hybridization may occur if particular reagents are present, etc. Clarification is required.

Claim Rejections - 35 U.S.C. § 103

8. Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Andersen et al in view of Ahern.

Andersen et al teach the nucleotide sequence of the *M. tuberculosis* L-alanine dehydrogenase gene, which comprises each of the sequences set forth in instant SEQ ID Nos 11-25 (see Andersen et al, Figure 5). Accordingly, it is a property of the molecule taught by Andersen et al that it is a nucleic acid consisting of a sequence that is "hybridizable" with each of the particular sequences recited in claim 1 under the conditions required by the claim. Andersen et al further teach that L-alanine dehydrogenase activity may be identified by employing a stain comprising NAD, L-alanine, PMS, and NBT (p. 2318). Accordingly, Andersen et al disclose methods for characterizing L-alanine dehydrogenase in which all the components set forth in claim 1 are employed. However, Andersen et al does not teach or suggest packaging NAD, L-alanine, PMS, and NBT into a kit, or suggest preparing a kit comprising this kit and their DNA molecule. Ahern teaches that pre-made reagents provided in kit form are convenient and save researchers time and money (see p. 3/5-4/5). In view of the teachings of Ahern, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the invention of Andersen et al so as to have packaged any or all of the reagents taught

by Andersen et al into a kit. An ordinary artisan would have been motivated to have made such a modification in order to have provided the reagents needed to perform Andersen et al's methods to practitioners in a convenient format for the advantages of efficiency and cost-effectiveness.

9. Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Andersen et al in view of Ahern, as applied to claim 1, above, and further in view of Innis et al ("Optimization of PCRs" in *PCR Protocols: a Guide to Methods and Applications*, Innis, M.A. et al, eds., Academic Press, Inc., San Diego, 1990, pages 3-12).

This rejection applies to the claim to the extent that it may be limited to kits comprising one or more nucleic acids consisting of the particular sequences set forth in the claim. The combined references of Andersen et al and Ahern do not teach nucleic acids consisting of the recited sequences. However, Andersen et al disclose that alanine dehydrogenase is expressed in some species of mycobacteria but not others, and teach that this protein has "potential relevance....for virulence and/or protection" (p. 2317). Accordingly, Andersen et al provide motivation to one of ordinary skill in the art to study alanine dehydrogenase gene structure and expression in different mycobacterial species. Further, Andersen et al suggest performing "genetic manipulations" in mycobacteria in order to inactivate alanine dehydrogenase and "get more information on the role of the enzyme in the metabolism and virulence of *M. tuberculosis*" (p. 2322). Thus, Andersen et al provide motivation to clone the alanine dehydrogenase gene or portions thereof so as to, e.g., construct clones for use in inactivation by homologous recombination. Innis et al disclose that PCR may be used to rapidly amplify nucleic acid targets of

interest from complex mixtures for further study by, e.g., visualization, screening, or sequencing (p. 3). Innis et al further disclose that a variety of primers meeting the general criteria set forth on page 9 of Innis et al may be used as "efficient primers". In view of the teachings of Andersen et al and Innis et al, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the alanine dehydrogenase nucleic acid of Andersen et al so as to have prepared fragments or subsequences thereof for use as primers in PCR amplification of mycobacterial alanine dehydrogenase genes. An ordinary artisan would have been motivated to have made such a modification in order to have rapidly cloned and/or sequenced alanine dehydrogenase genes from mycobacteria for the advantage of rapidly determining and studying the structure and expression of those genes and/or rapidly preparing clones for use in homologous recombination, as suggested by Andersen et al. Further, given the teachings of Innis et al, any primers consisting of portions of a known target molecule sequence (e.g., portions of the sequence taught by Andersen et al) and meeting Innis et al's general guidelines for "efficient primers", including the sequences set forth in instant claim 1, would be obvious to one of ordinary skill in the art. The present claim is not limited to, e.g., a particular primer pair with which unexpected results were obtained. Absent a showing of unexpected results, any primers consisting of subsequences of a known gene sequence and meeting known criteria for PCR primers are considered to be functionally equivalent for, e.g., amplification of that gene, and it would have been obvious to one of ordinary skill to have prepared such primers for that purpose. It is further noted that the claim as written is not limited to primers, but

encompasses probes consisting of the particular sequences recited in the claim. Absent a showing of unexpected results with probes that consist of particular subsequences of a gene sequence known in the art (e.g., the L-alanine dehydrogenase gene sequence taught by Andersen et al which comprises each of SEQ ID NOs 11-25), such probes are also considered to be functionally equivalent for, e.g., detection of the gene, and it would have been obvious to one of ordinary skill in the art at the time the invention was made to have prepared fragments of the nucleic acids of, e.g., Andersen et al, because such fragments would have been useful as probes.

Conclusion

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Diana Johannsen whose telephone number is 703/305-0761. The examiner can normally be reached on Monday-Friday from 7:00 a.m. to 3:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached at 703/308-1152. The fax phone number for the Technology Center where this application or proceeding is assigned is 703/305-3014 or 305-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703/308-0196.

Diana Johannsen

October 4, 2001

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600